Remarks

The Office Action mailed December 16, 2004 has been received and reviewed. Claims 13 and 15 having been amended, the pending claims are claims 1-15. Claims 9-12 being withdrawn from examination, as drawn to a non-elected inventions, claims 1-8 and 13-15 are currently under examination. Reconsideration and withdrawal of the rejections are respectfully requested.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claim 15 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner asserted that the identity of the "binding agent" of claim 15 was unclear. To clarify the claimed invention, Applicants have amended claim 15 to recite "wherein the binding agent of the bacteriophage comprising a binding agent is biotin and said ligand of the first substrate comprising immobilized ligand for the binding agent is streptavidin." In view of this clarification, Applicants respectfully request the withdrawal of the rejection of claim 15 under 35 U.S.C. §112, second paragraph.

The 35 U.S.C. §103 Rejection of claims 1-6 over Wilson in view of Olsvik and Sun

The Examiner rejected claims 1-6 under 35 U.S.C. §103(a) as being unpatentable over Wilson (U.S. Patent No. 5,985,596) in view of Olsvik et al. (*Clin. Microbiol. Rev*, 1994; *7*:43-54) and Sun et al. (*J. Industr. Micriobiol. Biotech.*, 2000;*25*:273-275). This rejection is respectfully traversed. To establish a *prima facie* case of obviousness, three basic criteria must be met. See MPEP § 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the references when combined must teach or suggest all the claim elements. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicants' disclosure. *In re*

Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Applicants respectfully submit that the Examiner has failed to establish these basic requirements of a *prima facie* case of obviousness in the rejection of claims 1-6 under 35 U.S.C. §103(a) as being unpatentable over Wilson in view of Olsvik et al. and Sun et al.

Requisite motivation to combine documents is absent

According to MPEP § 2143.01, "[o]bviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." With this rejection of claims 1-6 under 35 U.S.C. §103(a), the Examiner has provided no statement identifying why one of skill in the art would be motivated to combine the teachings of Wilson with the teachings of Olsvik et al. and Sun et al. (see pages 4-6 of Office Action mailed December 16, 2004). Further, Applicants respectfully submit that no motivation to combine the teachings of Wilson in view of Olsvik et al. and Sun et al. is to be found either in the teachings of Wilson, Olsvik et al., or Sun et al. themselves or in the knowledge generally available to one of ordinary skill in the art.

Wilson teaches a method for reducing the time of response to assay for a slow growing bacterium. The method taught by Wilson involves four steps (see abstract, col. 2, lines 18-37, and representative claim 1). First, a first bacterium is exposed to infection by a phage to which the first bacterium is permissive. Second, phage particles that have not been absorbed by the bacterium are inactivated or removed. The techniques for inactivating or removing phage particles disclosed include washing and filtering the sample to physically separate exogenous phage from the infected bacterial cells (col. 5, lines 65-67), treating the sample with an acid, a surfactant or a chemical to kill or render inactive the exogenous phage particles (col. 6, lines 1-3 and 7-34), or absorbing phage particles onto a substrate such as filter paper, by capillary action (col. 6, lines 3-6 and col. 9, lines 53-56). Third, the treated first bacterium is cultivated in the presence of second bacterium which is permissive to the phage and has a doubling rate greater than the effective doubling rate of the first bacterium. Fourth, the extent of plague formation and/or growth of the second bacterium is assessed.

Olsvik et al. teach magnetic separation techniques for use in diagnostic microbiology. The very limited teachings of Olsvik et al. relating to the detection of bacteriophage (referred to therein as "viruses") are limited to the use of oligonucleotide probes linked to magnetic beads to be used as primers in a polymerase chain reaction (PCR) for the direct detection of viral RNA or DNA in a sample by (see Oslvik et al. pages 50-51).

Applicants submit that one of ordinary skill in the art would not be motivated to combine the teachings of Wilson (on the detection of slow growing bacteria) with the teachings of Olsvik et al. (on the detection of viral RNA or viral DNA by PCR) to obtain the present invention. The Examiner has not identified such motivation, and Applicants respectfully submit such motivation is lacking. In discussing the combined teachings of Wilson and Oslvik et al, the Examiner asserted "that the methods proven useful for the detection of virus" taught in Oslvik et al. "would be the functional equivalent of the removal or inactivation of the phage as is taught by Wilson" (page 5, Office Action mailed December 16, 2004). Applicants adamantly disagree. Applicants submit that Oslvik et al. teach no methods for the removal or inactivation of phage in a sample and respectfully submit that the Examiner's assertion is incorrect.

Likewise, Applicants respectfully submit that one of ordinary skill in the art would not be motivated to combine the teachings of Wilson or Olsvik et al. with the teachings of Sun et al. to obtain the present invention. The teachings of Wilson, of a method comprising the physical removal or inactivation of bacteriophage within a sample, and the teachings of Oslvik et al, of the detection of viral DNA and RNA by PCR, have been summarized above. Sun et al. teach the construction of a biosorbent for the capture of *Salmonella enteritidis* bacterial cells from a sample. This biosorbent is formed by coating magnetic beads with bacteriophage specific for *S. enteritidis* via streptavidin-biotin interactions. Sun et al. teach the use of bacteriophage, as a replacement to antibodies for the capture and removal of bacterial cells from a sample (see abstract and Introduction, page 273 of Sun et al.). The teachings of Sun et al. are limited to the capture and removal of *bacterial cells* from a sample. Applicants respectfully submit that no motivation to combine the teachings of Wilson, on a method comprising the physical removal or inactivation of bacteriophage within a sample, and the teachings of Oslvik et al., on a method of detecting viral RNA or DNA by PCR, with teachings of Sun et al., on the construction of a biosorbent for the capture of bacterial cells from a sample, is to be found either explicitly or implicitly in the documents themselves or in the knowledge generally available to one of ordinary skill in the art.

Applicants respectfully submit that the requisite motivation to combine the teachings of Wilson in view of Olsvik et al. and Sun et al., to arrive at the claimed invention, is absent. Applicants submit that claims 1-6 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. Reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) is requested.

Examiner has used impermissible hindsight

As presented above, there is no teaching or motivation to combine the teachings Wilson in view of Olsvik et al. and Sun et al. Thus, Applicants respectfully submit that the Examiner's conclusion of obviousness is based on impermissible hindsight reasoning. "It is error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a 'blueprint.' When the prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than hindsight obtained from the invention itself." *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985). Applicants submit that the Examiner has engaged in the impermissible hindsight reconstruction of the claimed invention, using the Applicants' claims as a template and merely picking and choosing selected claim elements from the various documents. Applicants submit that claims 1-6 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. Withdrawal of this rejection is respectfully requested.

No reasonable expectation of success

According to MPEP § 2143.02, "[t]he prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants submit that one of ordinary skill in the art would not have a reasonable expectation of success in combining the disparate teachings of Wilson, Olsvik et al., and Sun et al. Thus, Applicants submit that claims 1-6 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. Reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) is requested.

Documents combined do not teach the claimed invention

According to MPEP § 2143.03, "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)." Claims 1-6 are drawn to:

> A method of detecting a bacterial cell in a sample comprising:
>
> contacting the sample with bacteriophage comprising a binding agent, wherein the bacteriophage is specific to the bacterial cell;
>
> incubating the sample under conditions effective for the bacteriophage comprising a binding agent to infect the bacterial cell, and if a bacterial cell is present in the sample and has been infected by the bacteriophage comprising a binding agent, form new bacteriophage and release new bacteriophage into the sample, wherein the new bacteriophage do not comprise a binding agent;
>
> contacting the sample with a substrate comprising immobilized ligand for the binding agent under conditions effective for a complex to form between the bacteriophage comprising a binding agent and the substrate comprising immobilized ligand for the binding agent;
>
> removing the complexes of bacteriophage comprising a binding agent and substrate comprising immobilized ligand from the sample; and
>
> detecting new bacteriophage in the sample from which complexes have been removed, wherein the presence of new bacteriophage indicates the presence of a

> bacterial cell specific for the bacteriophage in the sample and wherein the absence of new bacteriophage indicates the absence of a bacterial cell specific for the bacteriophage in the sample.

Applicants submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach each and every element of the claimed invention. Specifically, in the method of claims 1-6 a sample is contacted "*with bacteriophage comprising a binding agent.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach or suggest a "*bacteriophage comprising a binding agent,*" as recited in claims 1-6.

Further, in the method of claims 1-6 a sample is incubated under conditions effective to "*form new bacteriophage* and release new bacteriophage into the sample, *wherein the new bacteriophage do not comprise a binding agent.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach or suggest "*new bacteriophage [that] do not comprise a binding agent*" of claims 1-6.

The method of claims 1-6 comprises "contacting the sample with *a substrate comprising immobilized ligand for the binding agent* under conditions effective *for a complex to form between the bacteriophage comprising a binding agent and the substrate comprising immobilized ligand for the binding agent.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach or suggest a "*substrate comprising immobilized ligand for the binding agent*" of claims 1-6. Further, Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach or suggest forming a complex "*between the bacteriophage comprising a binding agent and the substrate comprising immobilized ligand for the binding agent,*" as recited in claims 1-6.

Further, the method of claims 1-6 comprises "*removing the complexes of bacteriophage comprising a binding agent and substrate comprising immobilized ligand from the sample.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach or suggest "*removing the complexes of bacteriophage comprising a binding agent and substrate comprising immobilized ligand from the sample,*" as recited in claims 1-6.

Finally, the method of claims 1-6 comprises "*detecting new bacteriophage*" (wherein the new bacteriophage do not comprise a binding agent). Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. do not teach or suggest detecting new bacteriophage, as recited in claims 1-6.

Thus, Applicants submit that Wilson in view of Olsvik et al. and Sun et al. do not teach each and every element of the method of claims 1-6. Claims 1–6 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. Reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) is respectfully requested.

Conclusion

In conclusion, Applicants respectfully submit that the requisite motivation to combine the teachings of Wilson in view of Olsvik et al. and Sun et al. is absent. Applicants submit that the Examiner's conclusion of obviousness is based on impermissible hindsight reasoning. Further, Applicants respectfully submit that there is not a reasonable expectation of success in combining the teachings of Wilson in view of Olsvik et al. and Sun et al. Finally, Applicants submit that Wilson in view of Olsvik et al. and Sun et al. do not teach each and every element of the claimed method. Thus, the Examiner has failed to establish the basic requirements of a *prima facie* case of obviousness in the rejection of claims 1-6 as being unpatentable over Wilson in view of Olsvik et al. and Sun et al. Reconsideration and withdrawal of this rejection of claims 1-6 under 35 U.S.C. §103(a) is respectfully requested.

The 35 U.S.C. §103 Rejection of claims 7 and 8 further in view of Teodorescu

The Examiner rejected claims 7 and 8 under 35 U.S.C. §103(a) as being unpatentable over Wilson, Olsvik et al. and Sun et al. as applied to claims 1-6, and further in view of Teodorescu et al. (U.S. Patent No. 4,797,363). This rejection is respectfully traversed. The deficiencies of Wilson, Olsvik et al., and Sun et al., as applied to claims 1-6, have been discussed above. Applicants respectfully submit that the teachings of Teodorescu et al. do not correct the deficiencies of Wilson, Olsvik et al., and Sun et al., as applied to claims 1-6.

Claims 7 and 8 are drawn to the method of claim 1 "wherein the new bacteriophage is detected using a fluorescent dye or fluorescent nanocrystals." Applicants submit that Teodorescu et al. do not teach the detection of new bacteriophage using a fluorescent dye or fluorescent nanocrystals and do not teach visualization under a light microscope. Thus, the combined teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Teodorescu et al. do not teach each and every element of the claimed invention. Further, Applicants respectfully submit that the requisite motivation to combine the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Teodorescu et al. to arrive at the claimed invention is absent. The Examiner has included no motivation statement in the Office Action and none can be found in the teachings of Wilson, Olsvik et al., Sun et al., or Teodorescu et al. Again, the Examiner has engaged in the impermissible hindsight reconstruction of the claimed invention, using Applicants' claims as a template and merely picking and choosing elements from the various documents to fill the gaps. Applicants respectfully submit that claims 7 and 8 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. as applied to claims 1-6 and further in view of Teodorescu et al. Reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) is requested.

The 35 U.S.C. §103 Rejection of claims 13-15 over Wilson in view of Olsvik and Sun and further in view of Yazdankhah

The Examiner rejected claims 13-15 under 35 U.S.C. §103(a) as being unpatentable over Wilson, Olsvik et al., and Sun et al. as to claims 1-6, and further in view of Yazdankhah et al. (*Vet. Microbiol.*, 1998; *62*:17-26). This rejection is respectfully traversed. The deficiencies of Wilson, Olsvik et al., and Sun et al., as applied to claims 1-6, have been discussed above. Applicants respectfully submit that the teachings of Yazdankhah et al. do not correct the deficiencies of Wilson, Olsvik et al., and Sun et al. as applied to claims 1-6.

Further, Applicants submit that the requisite motivation to combine the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. is lacking. The Examiner's Office Action provides no statement of motivation to combine the cited teachings. And, Applicants submit that one of ordinary skill in the art would not be motivated to combine the teachings of Yazdankhah et al. (teaching a method of detecting *Staphylococcus* bacteria in milk samples by the use of magnetic beads coated with monoclonal antibodies specific to the *Staphylococcus* bacteria) with the teachings of Wilson (teaching a method of assaying for a slow growing bacterium by exposing a first bacterium to infection by a phage, inactivating phage particles that have not been absorbed by the first bacterium, cultivating the first bacterium in the presence of a second bacterium, and assessing the extent of plague formation and/or growth of the second bacterium), the teachings of Olsvik et al. (teaching the direct detection of viral RNA or DNA in a sample by the use of oligonucleotide probes linked to magnetic beads as primers in polymerase chain reactions), and the teachings of Sun et al. (teaching the construction of a biosorbent for the capture of bacterial cells within a sample). As there is no motivation to combine the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al., Applicants submit that the Examiner has engaged in the impermissible hindsight reconstruction of the claimed invention.

Finally, Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach each and every element of the method of claims 13-15. In the method of claims 13-15 a sample is contacted "*with bacteriophage comprising a binding agent.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach or suggest a "*bacteriophage comprising a binding agent.*" In claims 13-15 the sample is incubated under conditions effective to "*form new bacteriophage* and release new bacteriophage into the sample, *wherein the new bacteriophage do not comprise a binding agent.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach or suggest "*new bacteriophage [that] do not comprise a binding agent.*"

The method of claims 13-15 comprises "contacting the sample with *a first substrate comprising immobilized ligand for the binding agent* under conditions effective for a *complex to form between the bacteriophage comprising the binding agent and the first substrate* *comprising immobilized ligand for the binding agent.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach or suggest a "*a first substrate comprising immobilized ligand for the binding agent.*" Further, Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach or suggest forming a "*complex between the bacteriophage comprising the binding agent and the first substrate comprising immobilized ligand for the binding agent.*"

The method of claims 13-15 comprises "*removing the complexes of bacteriophage comprising a binding agent and first substrate comprising immobilized ligand from the sample.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach or suggest the *"removing the complexes of bacteriophage comprising a binding agent and first substrate comprising immobilized ligand from the sample,*" as recited in claims 13-15.

Further, the method of claims 13-15 comprises "contacting the sample with a second substrate comprising immobilized binding agent specific for the new bacteriophage, under conditions effective for *a complex to form between the new bacteriophage and the second substrate comprising immobilized binding agent for the new bacteriophage.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach "*contacting the sample with a second substrate comprising immobilized binding agent specific for the new bacteriophage*" and do not teach the formation of "*a complex to form between the new bacteriophage and the second substrate comprising immobilized binding agent for the new bacteriophage,*" as recited in claims 13-15.

And further, the method of claims 13-15 comprises "*removing the complexes of new bacteriophage and second substrate comprising immobilized binding agent for the new bacteriophage.*" Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach "*removing the complexes of new bacteriophage and second substrate comprising immobilized binding agent for the new bacteriophage,*" as recited in claims 13-15.

Finally, the method of claims 13-15 comprises "*detecting the complexes of new bacteriophage and second substrate comprising immobilized binding agent for the new bacteriophage*." Applicants respectfully submit that the teachings of Wilson in view of Olsvik et al. and Sun et al. and further in view of Yazdankhah et al. do not teach "*detecting the complexes of new bacteriophage and second substrate comprising immobilized binding agent for the new bacteriophage*," as recited in claims 13-15.

Thus, Applicants submit that Wilson in view of Olsvik et al. and Sun et al. and further in view of further in view of Yazdankhah et al. do not teach each and every element of the method of claims 13-15. Claims 13-15 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. and further in view of further in view of Yazdankhah et al.

In conclusion, in view of the above discussion, Applicants submit that claims 13-15 are not *prima facie* obvious over Wilson in view of Olsvik et al. and Sun et al. further in view of Yazdankhah et al. Reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) is requested.

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Summary

It is respectfully submitted that the pending claims 1-15 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the below-listed telephone number if it is believed that prosecution of this application may be assisted thereby.

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